PATENT COOPERATION TREATY

PCT

Appl. No. 10/594,436
Doc. Ref. NPL4

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference ESRN-008PC	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/IB2007/004315	International filing date *(day/month/year)* 04 October 2007 (04.10.2007)	Priority date *(day/month/year)* 06 October 2006 (06.10.2006)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant EISAI R&D MANAGEMENT CO., LTD		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 10 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☒	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 07 April 2009 (07.04.2009)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Cecile Chatel e-mail: ro.ib@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2007/004315	04.10.2007	06.10.2006

International Patent Classification (IPC) or both national classification and IPC
INV. A61K9/48 A61K31/4439

Applicant
EISAI CO., LTD.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Date of completion of this opinion
see form PCT/ISA/210

Authorized Officer
Gómez Gallardo, S

Telephone No. +31 70 340-9546

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB2007/004315

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing:

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in electronic form.

      ☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. II Priority

1. ☐ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.

2. ☒ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-14
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-14
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

CITED DOCUMENTS

Reference is made to the following documents:

D1: US-B1-6 174 902 (YELLE WILLIAM E [US] ET AL) 16 January 2001 (2001-01-16)

D2: WO 2005/027880 A (NATCO PHARMA LTD [IN]) 31 March 2005 (2005-03-31)

D3: WO 2006/011159 A (TORRENT PHARMACEUTICALS LTD [IN]) 2 February 2006 (2006-02-02)

D4: OHNING G V ET AL: "Rabeprazole produces rapid, potent, and long-acting inhibition of gastric acid secretion in subjects with Helicobacter pylori infection" ALIMENTARY PHARMACOLOGY & THERAPEUTICS, BLACKWELL SCIENTIFIC PUBLICATIONS LTD., CAMBRIDGE, GB, vol. 14, no. 6, 1 June 2000 (2000-06-01), pages 701-708, XP002487514 ISSN: 0269-2813

D5: LEW E A: "Review article: pharmacokinetic concerns in the selection of anti-ulcer therapy" ALIMENTARY PHARMACOLOGY & THERAPEUTICS, BLACKWELL SCIENTIFIC PUBLICATIONS LTD., CAMBRIDGE, GB, vol. 13 Suppl 5, 1 October 1999 (1999-10-01), pages 11-16, XP002375912 ISSN: 0269-2813

D6: LEW E A ET AL: "An ascending single-dose safety and tolerance study of an oral formulation of rabeprazole (E3810)" ALIMENTARY PHARMACOLOGY & THERAPEUTICS, vol. 12, no. 7, 1998, pages 667-672, XP002497041

D7: YASUDA S ET AL: "Pharmacokinetic properties of E3810, a new proton pump inhibitor, in healthy male volunteers" INT J CLIN PHARMACOL THER, vol. 32, no. 9, 1994, pages 466-473, XP008096717

D8: EP-A-1 454 634 (EISAI CO LTD [JP] EISAI R & D MAN CO LTD [JP]) 8 September 2004 (2004-09-08)

D9: WO 2006/042277 A (EISAI CO LTD [JP]) 20 April 2006 (2006-04-20)

D10: WO 2004/066982 A (RANBAXY LAB LTD [IN]) 12 August 2004 (2004-08-12)

D11: EP-A-1 930 030 (EISAI R & D MAN CO LTD [JP]) 11 June 2008 (2008-06-11) (& WO 2007/037259 (EISAI R & D MAN CO LTD [JP]) 5 April 2007 (2007-04-05); of the same family)

D12: WO 2007/072503 A (PANACEA BIOTEC LTD [IN]) 28 June 2007 (2007-06-28)

Re Item II

Priority

Earlier applications EP-A-1 930 030 A (D11a) and WO 2007/037259 (D11b) published on 11 June 2008 and 5 April 2007, respectively, claim the priority date of 29 September 2005. They disclose (cf. passages in the search report) a pulsed-release capsule comprising 6 tablets of rabeprazole sodium, each tablet comprising 10 mg of active. Therefore, in total, the capsule comprises 60 mg of rabeprazole sodium.

The application US 60/850,023 (date of filing 6 October 2006), to which the priority claim of the present application is directed, is, therefore, not the application disclosing for the first time some of the subject-matter of the present PCT application. As some of the subject-matter, as described above, was disclosed in the still earlier applications D11a and D11b originating from the same applicant (EISAI CO., LTD.), the application US 60/850,023 is in fact not the "first application". Therefore, the priority claim is invalid for the subject-matter already disclosed in the still earlier applications D11a and D11b and documents D11b and D12 will be considered as forming part of the prior art according to Art. 33(2) PCT.

Re Item V

Reasoned statement with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. CLARITY (Art. 6 PCT)

1.1. Claims 1, 7 and 13 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the formulation in terms of a **result to be achieved**, namely as providing extended release. This merely amounts to a statement of the underlying problem, **without providing the technical features** (i.e. the components of the formulation and their amount) **necessary for achieving this result**. In view of this, all of the formulations disclosed in D1-D7, D11b and D12 are, at present, considered as novelty destroying for the above-mentioned claims.

1.2. Claims 1, 7-9 and 13 refer to the pharmacokinetic parameters C_{max} and AUC, which have been assessed in-vivo. In-vivo tests, however, not only depend on the dosage form but also

on the patient to whom this dosage form is administered. In other words, C_{max} and AUC depend on factors such as age, gender, renal and hepatic impairment, concomitant diseases, etc. As a consequence, they are considered as unreliable parameters since the skilled person performing an in-vivo test using a dosage form does not know whether (s)he is working inside or outside the scope of the claim because (s)he might obtain a different result with the same product but with another patient or even the same patient at a different time. Therefore, claims 1, 7-9 and 13 are unclear and do not meet the requirements of Article 6 PCT. Also, in view of the above-mentioned objection, the attention of the applicant is drawn to the fact that **said parameters are not taken into account when evaluating the novelty of the present application.**

2. NOVELTY (Art. 33(2) PCT)

The present application does not meet the criteria of Article 33(1) PCT because the subject-matter of claims 1-14 is not new in the sense of Article 33(2) PCT.

Document D1 discloses (cf. column 3, lines 16-24) an oral composition in the form of a tablet or a capsule comprising 10, 30 or 50 mg of rabeprazole. In particular, examples 2 and 3 (cf. column 6 - column 7) disclose enteric coated granules comprising 30 mg of rabeprazole, said granules being filled into capsules. Therefore, the subject-matter of claims 1-14 is not new in view of D1.

Document D2 discloses (cf. page 9, lines 18-20) capsules comprising from 5 to 100 mg, preferably from 10 to 40 mg, of rabeprazole. In particular, example 6 (cf. page 16 - page 17) discloses a capsule comprising 40 mg of rabeprazole sodium. Therefore, the subject-matter of claims 1, 2, 5-10, 13 and 14 is not new in view of D2.

Document D3 discloses (cf. page 11, paragraph 7; page 15, last paragraph - page 18, paragraph 1) enteric coated pellets comprising from 5 to 100 mg, preferably from 10 to 40 mg, of rabeprazole sodium. Said pellets can be filled in a capsule. Therefore, the subject-matter of claims 1, 2, 5-10, 13 and 14 is not new in view of D3.

Document D4 discloses (cf. abstract; page 706, table 4) an oral composition comprising 40

mg of rabeprazole. Therefore, the subject-matter of claims 1, 2, 7-10, 13 and 14 is not new in view of D4.

Document D5 discloses (cf. abstract; page 12, right-hand column, paragraph 3; page 13, figure 2 and table 1) an oral composition comprising 40 mg or 80 mg of rabeprazole. Therefore, the subject-matter of claims 1, 2, 4, 7-10 and 12-14 is not new in view of D5.

Document D6 discloses (cf. abstract; page 668, left-hand column, paragraph 3 - right-hand column, paragraph 1; page 670, table 2; page 670, right-hand column, paragraph 2 - page 671, left-hand column, paragraph 3) an oral composition comprising 30 mg or 40 mg of rabeprazole sodium. Therefore, the subject-matter of claims 1, 2, 6-10, 13 and 14 is not new in view of D6.

Document D7 discloses (cf. abstract; page 467, right-hand column, last paragraph; page 469, figure 2; page 470, table 1) an oral composition comprising 40 mg or 80 mg of rabeprazole sodium. Therefore, the subject-matter of claims 1, 2, 4, 6-10 and 12-14 is not new in view of D7.

Document D11b discloses (cf. same corresponding passages given in the search report for D11a) a pulsed-release capsule comprising 60 mg of rabeprazole sodium in the form of 6 tablets, each tablet comprising 10 mg of active. Therefore, the subject-matter of claims 1-14 is not new in view of D11b.

Document D12 discloses (cf. page 23, example 5) a capsule comprising 40 mg of rabeprazole. Therefore, the subject-matter of claims 1, 2, 5-10, 13 and 14 is not new in view of D12.

3. INVENTIVE STEP (Art. 33(3) PCT)

3.1. Claims 1-14 being not new are also not inventive (Art. 33(3) PCT).

3.2. The attention of the applicant is also drawn to the relevance of documents D8 and D9 with regard to the inventive step of the present application (Art. 33(3) PCT). These documents

disclose (cf. passages in the search report) extended release compositions comprising rabeprazole. The amount of rabeprazole is not explicitly disclosed. However, no unexpected effect and, therefore, no inventive step seem to be related to the amount of rabeprazole in the formulation being from 30 to 90 mg (Art. 33(3) PCT). The relevance of D10 is also to be noted since the example 3 of this document discloses (cf. page 16 - page 17) tablets with an intermediate coating and an enteric coating, said tablets comprising 10 mg of rabeprazole. It is stated in said example that "multiple" tablets are filled in capsules. With respect to D10, an amount of 30 to 90 mg of rabeprazole would merely consist in the selection of a particular range of mg of active contained in the capsules (i.e. a particular amount of tablets to be filled in the capsules). Such a selection could only be regarded as inventive, if the amount between 30 and 90 mg would present unexpected effects or properties in relation to the rest of the range. However, no such effects or properties are indicated in the application (Art. 33(3) PCT).

4. INDUSTRIAL APPLICABILITY (Art. 33(4) PCT)

Claims 1-14 satisfy the criterion of industrial applicability set forth in Article 33(4) PCT.

Re Item VI
Certain documents cited

Certain published documents

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO 2008/067037	05/06/2008	05/10/2007	05/10/2006
WO 2008/002567	03/01/2008	26/06/2007	27/06/2006

Re Item VIII
Certain observations on the international application

CLARITY (Art. 6 PCT)

Although claims 1, 7 and 13 have been drafted as **separate independent claims**, they appear to relate effectively to the same subject-matter and to differ from each other only with

regard to the definition of the subject-matter for which protection is sought and/or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore **lack conciseness** and as such do not meet the requirements of Article 6 PCT.